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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,054	.04/29/2002	Eric Lam	RU-0175	4375
26259	7590	08/29/2005	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			MEHTA, ASHWIN D	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/009,054	Applicant(s) LAM, ERIC	
	Examiner Ashwin Mehta	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 April 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. The rejection of claims 1-32 under 35 U.S.C. 112, second paragraph is withdrawn in light of the claim amendments.

Claim Rejections - 35 USC § 112

3. Claims 24-32 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA construct for integration of heterologous DNA segment into genomes, wherein the DNA construct is adapted for integrating a heterologous DNA segment at a pre-determined location in the Chlamydomonas genome, and a method for inserting a heterologous DNA molecule into a pre-determined location of a Chlamydomonas genome, does not reasonably provide enablement for DNA constructs adapted for integrating a heterologous DNA segment into pre-determined locations of other plant genomes, or methods for inserting a heterologous DNA into a pre-determined location in other plant genomes, or a method of activation tagging of a plant genome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record stated in the previous Office actions. Applicant traverses the rejection in the paper filed June 13, 2005. Applicant's arguments were fully considered but were not found persuasive.

Applicant argues that Puchta teaches that gene targeting in plants such as *Arabidopsis* and *Physcomitrella* was achieved at the time of filing, albeit not efficiently, and that the necessary techniques for preparing constructs, transforming plant cells, and screening for gene targeting events were well-known at the time of filing (response, paragraph bridging pages 11-12). However, one of Puchta's conclusions is "Time will tell when and by which approach gene targeting in higher plants will be achieved in a feasible way" (page 180). That success of gene targeting in *Physcomitrella* is not representative of success in all other species. Puchta addresses the question of why gene targeting occurs in *Physcomitrella patens* and not higher plants, but did not propose any conclusions. Rather, Puchta teaches that further studies are needed to gain a deeper understanding (paragraph bridging pages 179-180). Applicants argue that the level of one of ordinary skill was quite high, and cite the teachings of Miao and Lam (response, page 12, 1st full paragraph). Miao et al. discuss homologous recombination in *Arabidopsis*, involving the *AGL5* gene. However, as discussed in the previous Office actions, Puchta teaches that the results of the homologous recombination experiments with *Arabidopsis* of Miao and Lam were controversial and, for the years that followed, no further successful gene targeting experiments were reported (paragraph bridging pages 174-175). If an experiment cannot be repeated by others in the art, it cannot be said to be routine or within the level of one skilled in the art.

Regarding predictability, Applicants argue that Puchta teaches that a gene targeting event could be obtained at a frequency of 1 out of every 10,000 to 100,000 random integration events. While admitting that this is a high number of transformants to screen, Applicants argue that this type of screening is routine and predictable in the art (response, page 12, last paragraph). However, frequencies of 1 in 10,000 to 100,000 were not considered to define a feasible gene

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targeting technique useful in the art. Puchta teaches that attempts to improve this ratio did not result in significantly higher frequencies (page 174). Puchta states that a number of approaches were developed recently that *might* lead to a feasible gene targeting technique in the near future (emphasis added; page 173). This is a clear indication that feasible gene targeting techniques in higher plants still required undue experimentation for their development in the art at the time of filing of the instant application.

Applicants argue that the specification provides guidance as to how to carry out the integration of a heterologous DNA at a predetermined location on a plant genome, discloses the necessary elements of a gene targeting construct, and how to select for desired homologous recombination events, and that a prophetic example is provided (response, page 13, 1st and 2nd full paragraphs). Applicants argue that the amount of guidance provided is such that the amount of experimentation is undue, and that the basis of the instant invention is to improve upon existing techniques, and that the art has established that homologous recombination occurs in plants (response, paragraph bridging pages 13-14 and page 14, 1st full paragraph). However, the specification does not teach how to overcome the deficiencies of gene targeting at predetermined locations that hampered those skilled in the art at the time of filing. The prophetic example in the specification fails to teach any improvements over the prior art, which does not teach a feasible gene targeting technique for higher plants.

Claim Rejections - 35 USC § 103

4. Claims 1-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yoder et al. (WO 92/01370) in view of Hashimoto et al. (Plant Sci., February 1999, Vol. 141, pages 175-

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181), Bayley et al. (Plant Mol. Biol., 1992, Vol. 18, pages 353-361), and Suter-Crazzolara et al. (Meth. Cell Biol., 1995, Vol. 50, pages 425-438), for the reasons of record stated in the previous Office action. Applicant traverses the rejection in the paper filed June 13, 2005. Applicant's arguments were fully considered but were not found persuasive.

Applicants argue that MPEP 2143.01 indicates that indicates that the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination, and that the courts have held that a suggestion or motivation to modify must be in a reference (response, page 16, 1st full paragraph). However, the motivation to combine references need not be stated in a prior art reference. MPEP 2143.01 states, "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998)". MPEP 2144 also states, "The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law."

Applicants argue that Yoder do not contemplate the use of two selectable markers, and that the secondary references fail to teach or suggest positive and negative selection markers in a DNA construct, and as such the references fail to teach all of the limitations of the instant claims (response, paragraph bridging pages 16-17). However, the combined references do teach the

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elements required to be present in the DNA construct of the instant claims, including negative and positive selection markers.

5. Claims 29-32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yoder et al. in view of Hashimoto et al., Bayley et al., and Suter-Crazzolara et al. as applied to claims 1-23 above, and further in view of Walden et al. (Plant Mol. Biol., 1994, Vol. 26, pages 1521-1528), for the reasons of record stated in the previous Office action. Applicant traverses the rejection in the paper filed June 13, 2005. Applicant's arguments were fully considered but were not found persuasive.

Applicants argue that claims 29-32 are not obvious since parent claim 1 is not obvious, for the reasons presented for the rejection of claims 1-23 (response, page 18, 1st full paragraph). However, claim 1 is obvious over Yoder et al. in view of Hashimoto et al., Bayley et al., and Suter-Crazzolara et al., as discussed above.

Summary

6. Claims 1-32 remain rejected.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

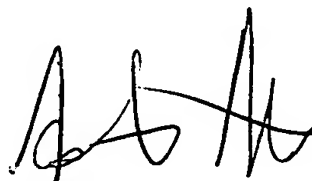
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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M. to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Jones, can be reached at 571-272-0745. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638

August 25, 2005